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OVERNIGHT COURIER 1/4/05

Division of Dockets Management
Food and Drug Administration (HFA-305)
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

CITIZEN PETITION

Dear Sir or Madam:

The undersigned submits this petition, in quadruplicate, pursuant to Section 505(j)(2)(C) of the Federal Food, Drug and Cosmetic Act and in accordance with 21 CFR 10.30 on behalf of a client requesting the Commissioner of the Food and Drug Administration to declare that the drug product, Risperidone Orally Disintegrating Tablets, 0.25 mg, is suitable for consideration in an abbreviated new drug application (ANDA).

A. Action Requested

The petitioner requests that the Commissioner of the Food and Drug Administration declare that the drug product Risperidone Orally Disintegrating Tablets 0.25 mg is suitable for submission in an ANDA. The listed reference drug product upon which this petition is based is Risperdal® M-Tab™ Orally Disintegrating Tablets (risperidone), 1 mg (also approved and available in 0.5 mg and 2 mg strengths and on December 23, 2004 also approved in strengths of 3 mg and 4 mg). Therefore, the petitioner seeks a change in strength (from the currently approved 1 mg RLD and 0.5 mg 2 mg, 3 mg and 4mg orally disintegrating tablets to include a 0.25 mg strength of the orally disintegrating tablet) from that of the listed drug product.

B. Statement of Grounds

The reference-listed drug (RLD) product (Risperdal® M-Tab™) is currently available in approved tablet strengths of 0.5 mg, 1 mg, 2 mg, 3 mg and 4 mg Orally Disintegrating Tablets (ODT) containing risperidone. A copy of the listing from the *Approved Drug Products with Therapeutic Equivalence Evaluations* 24th edition is included in Attachment 1 (page 3-311). (Note that the approvals of the 3 mg and 4 mg strengths are so recent that they are not yet listed in the Orange Book.) The proposed drug product represents an orally disintegrating tablet that will contain a lower strength of the drug (0.25 mg). This lower strength is, however, consistent with and clearly contemplated in the currently approved RLD product's labeling and it is also an approved strength of Risperdal Tablets (immediate-release (IR)). The IR product is currently approved in the following strengths: 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg and 4 mg.

The labeling of the RLD, which is a combined insert for the IR tablets, the oral solution, and the orally disintegrating tablets states:

> "Pharmacokinetic studies showed that RISPERDAL® M-TAB™ Orally Disintegrating Tablets are bioequivalent to RISPERDAL® Tablets."

Therefore, since the IR tablets and the orally dissolving tablets are bioequivalent, the strengths for one of the products are thus clearly contemplated for the other.

The inclusion of this additional strength in the orally disintegrating format will provide greater flexibility for the physician in providing a patient with the required dose in a orally disintegrating tablet and will represent a more convenient single tablet dosage unit to provide the specific dose prescribed by the physician for an individual patient that prefers the orally disintegrating tablet. The petition is thus seeking a change in strength (from the approved 0.5 mg, 1 mg, 2 mg, 3 mg and 4 mg ODT products to include a 0.25 mg strength of the ODT formulation) from that of the reference-listed drug.

The RLD product's labeling provides for various dosing regimens depending on the disease state and the response of the patients. Dosing can be from 1 mg to 16 mg per day in divided doses. Most patients are started on 1 mg twice daily with dosage adjustments made with weekly upward adjustment of usually 1 mg twice a day. The labeling does, however, indicate that some patients require slower titration or dosing depending on their individual response to the drug, hence, the various lower incremental dosage strengths (the approved 0.5 mg and proposed 0.25 mg).

Therefore, the petitioner is seeking changes in strength from the RLD drug product to provide the patient and physician with a more convenient single dosage strength of the orally disintegrating tablet to provide the full range of doses that are consistent with the approved strengths of the immediate-release tablet, and thus, clearly contemplated by the approved labeling of the RLD. With the orally disintegrating product being bioequivalent to the IR tablet product, including all strengths for the ODT product is appropriate. This will improve patient convenience, compliance and make it easier to achieve the required dose for those patients for whom the orally disintegrating formulation was found appropriate by the prescribing physician.

Copies of labeling of the reference-listed drug product upon which this petition is based and draft labeling for the proposed product are included in Attachment 2 and Attachment 3, respectively. Please note that the draft labeling for the proposed product will be revised to include the inactive ingredients and a complete How Supplied section when the ANDA is submitted. The proposed labeling is the "same as" the approved RLD labeling with the exception of changes allowed because the manufacturer of the generic product differs from that of the RLD and in the Description section and How Supplied section (when included which will list the additional available strength (0.25 mg) sought by this petition). There are no changes in the Indications or Dosage and Administration sections necessary as the approved labeling of the RLD already clearly contemplates and explicitly states the use of the proposed dosage strengths.

Because this petition requests only a change in strength from the listed drug, there is no requirement to request a waiver from the conduct of pediatric studies in accord with the Pediatric Research Equity Act of 2003.

Therefore, the petitioner requests that the Commissioner find that a change in strength from the 1 mg RLD (also approved in strengths of 0.5 mg, 2 mg, 3 mg and 4 mg) orally disintegrating tablet to include a 0.25 mg strength orally disintegrating tablet for this product raises no questions of safety or effectiveness, and the Agency should then approve the petition.

C. Environmental Impact

The petitioner claims a categorical exclusion under 21 CFR 25.31.

D. Economic Impact

The petitioner does not believe that this is applicable in this case, but will agree to provide such an analysis if requested by the Agency.

E. Certification

The undersigned certifies, that to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner, which are unfavorable to the petition.

Respectfully submitted,

Robert Pollock pk

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RWP/pk

Attachments:
1. *Approved Drug Products with Therapeutic Equivalence Evaluations,* 24th edition (page 3-311)
2. Labeling of the reference-listed drug product
3. Draft labeling for the proposed product

cc: Emily Thomas (OGD)

K09P5004